being lined with endothelial cells or not. The fact, however, that the children operated upon have improved and are still improving is of such significance to warrant the assumption that at least the artificial canals in the cerebral cortex are still patent.

With the exception of 6 of the total 28 children living after this operation of drainage, all of them have improved and are still improving; 5 of them have improved mentally and physically in every way, all of these children having been operated within one year after birth; 7 of the patients unable to walk before the operation are now walking, although with difficulty. The different stages of papillo-edema and choking of the optic disks producing a secondary optic atrophy and the visual impairment in these patients have been improved in each case unless a complete secondary optic atrophy had already occured.

Naturally, sufficient time has not yet elapsed to permit an opinion regarding the permanency of this improvement, and whether any of the younger patients will be normal and remain normal: but I do feel that the operative method here used does offer a chance of improvement to a large number of patients formerly considered hopeless; if a definite improvement can be obtained in the older children, then surely an earlier operation in the younger children when the condition is first observed and before the brain has been permanently damaged, should make a more hopeful prognosis possible. I am deeply indebted to Drs. McHenry and Hunt for their assistance; also to Dr. Lott for the apparatus devised by him to insert the linen strands into the ventricle; a description of it and the technic will be described in detail later.

EFFECT OF NUCLEIN INJECTION UPON THE LEUKOCYTES OF DOGS.

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AND

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The result of work upon the effect of nuclein in experimental animals has not been uniform, probably because under this name both the acid and its sodium salt have been employed and no standardization has been attempted. In approaching this subject, we determined to employ the product accepted by the American

Medical Association, nucleinic acid or its sodium salt, and to use the phosphorus percentage as our guide.

In counting blood cells three pipettes were prepared for each count, three chambers counted of each pipette, and the number of leukocytes calculated from the average. Differential counts were made of 400 cells in each case.

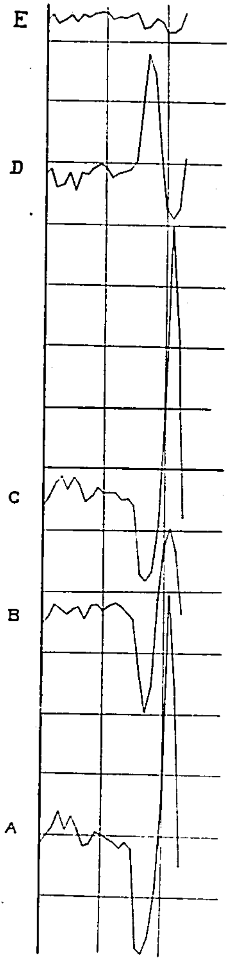
Counts were made immediately before the injection, and after the lapse of ½ hour, 1 hour, 2 hours, 4 hours, 7½ hours, 24 hours, 48 hours, 72 hours, and in some cases 96 hours after the injection. The effect of repeated puncturing of the dog's nose was controlled by taking counts on several untreated dogs. The effect of the injection of the menstruum in which the nuclein was to be administered was controlled by making counts after the intravenous and subcutaneous injection of physiological salt solution and 15 per cent. alcohol. The sodium nucleinate solution was prepared in 15 per cent. alcohol and physiological saline, in every case immediately before injection, and an amount of nuclein equivalent to 0.5 mg. phosphorus per kilo of dog weight was injected subcutaneously and intravenously in solution, 1 c.c. of which was equivalent to 1 mg. of phosphorus. The dog with which most work was done was a female of the fox terrier type, varying in weight from 7 kilos to 10 kilos in five months; of 24 counts taken in that time without treatment, the lowest was 7000 and the highest 13,000.

The injection of alcohol or of physiological salt solution, either intravenously or subcutaneously, was followed by no variation that did not fall within normal limits.

After the injection of sodium nucleinate, whether in 15 per cent. alcohol or physiological salt solution, whether subcutaneously or intravenously, there is a primary fall in the whole number of peripherally circulating leukocytes. This reaches its lowest point between the first and second hour, after which it starts to rise. The count is back to normal between four and seven hours, but the rise continues, until at the end of twenty-four hours the highest point is reached. From the twenty-fourth hour there is a gradual decline, the normal being reached between the seventy-second and ninety-sixth hour. In every experiment the curve greatly exceeded any figure for a similar period without treatment. The results of intravenous and subcutaneous injections are comparable, the clearness of the results, however, being greater by the former method.

Renner was able to raise the leukocytes 452 per cent. in his highest human case. Our greatest increase in the dog has been 290 per cent. of the original count.

The differential counts show after nuclein injection a relative and absolute decrease of polymorphonuclear neutrophiles, followed by a rise. This fall and rise of the polynuclear is largely responsible for the fall and rise of the whole count. Accompanying this curve of the polynuclears there is a similar downward and upward course



The curves are drawn to scale. *A*, variations in total number of white blood cells; *B*, variations in the per cent. of polymorphonuclear neutrophiles; *C*, variations in the number of polymorphonuclear neutrophiles; *D*, variations in the per cent. of small lymphocytes; *E*, variations in the number of small lymphocytes.

of the small lymphocytes, but it is of much less marked degree and more variable in its percentage; so much so, indeed, that no definite curve can be platted which will be followed in every experiment. In every case, however, the percentage of lymphocytes rises as the percentage of the polynuclears falls, and falls as it rises. This in itself shows that the gross variations in the total count must be due to polynuclear fall and rise. We are not now prepared to discuss the variations of the other leukocytes.

In a dog with an orginal leukocytosis and an eosinophilia the effect of the nuclein was the same as in the case of dogs with a normal blood picture.

In order to see if daily or twice daily injections of nuclein in 15 per cent. alcohol subcutaneously in quantities equivalent to 0.1 mg. of phosphorus per kilo would increase the leukocytes continuously and maintain them at a high level, a dog was given this treatment. There was a trifling rise of the whole number and of the percentage (therefore also the absolute number) of polynuclears. There was no continued rise, and the increase was irregular. This line of experimentation will be pursued further.

The Arneth formula in dogs is about as follows: 18, 40, 30, 7, 3. The injection of alcohol and saline has no appreciable effect upon it. Following an injection of nuclein, especially when given into the vein, there is a great relative and numerical increase of Type 1, cells with a single nucleus, amounting in one case to 52 per cent. of the polynuclears, while Type 2 remains about as normal and Types 3, 4, and 5 decrease. The rise of Type 1 seems to reach a high point in four hours corresponding to the time at which the leukocytes are on the increase and remains during the period in which the polynuclears are rising. Types 3 and 4 experience a fall roughly corresponding to the rise of Type 1, and later, corresponding again to the fall of Type 1, show a distinct increase, this arriving about the time that the leukocytes have resumed their usual numbers.

Nucleated reds have been encountered very occasionally in normal blood. After the injection of nuclein subcutaneously they are slightly increased, but when the substance is given into the vein they are increased quite markedly, in one case rising to eight times the number before injection. This rise appears during the time the leukocytes are falling. From a few observations it does not seem that there is any reduction in the number of red blood cells.

In 4 cases general toxic effects were noted after the intravenous injection of nuclein. The dogs became very restless for a few minutes, then lay quiet but trembling on the floor. After one and a half hours there was vomiting of a frothy yellow material, which vomiting was repeated throughout the day. On one occasion there were no general toxic symptoms.

Tentative conclusions from this work are that after nuclein injection there is a reduction in the circulating peripheral leukocytes, chiefly of the polymorphonuclears, and to a much less degree of the small lymphocytes, followed by a rise in both, but very largely of the polynuclears, even to 95 per cent. of the whole count. The total leukocyte count in dogs may be increased 290 per cent. in twenty-four hours. Repeated small doses of nuclein do not cause and maintain a high tide of leukocytosis. There seems to be destruction of polynuclears because of their great decrease, and the relative and absolute increase of young forms on the left side of Arneth's formula. The appearance of these young forms and of an increase in nucleated reds speaks for an increased activity of the bone marrow, therefore a stimulation of the tissue, but whether by the nuclein injected, as a response to the paucity of circulating white cells, or by excitation by the detritus of destroyed leukocytes we have not yet determined.

REFERENCES.

Gruber and Futaki. München. med. Wchnschr., 1906 and 1907.
Rosenow. Jour. Infect. Dis., vii, 411.
Schneider. Zeitsch. f. Hygiene, lxx and lxxv.
Petterson. Zent. f. Bakt., etc., xxxix, xlii, xlv, xlvi, l, liv, lx.
Horder. Quoted by Rosenow.
Hiss and Zinsser. Jour. Med. Res., xix and xiv.
Fox. Zent. f. Bakt., etc., lxx, 143.
Hofbauer. Arch. f. Gynäk., 1903, lxviii, 359.
Ames and Huntley. Jour. Am. Med. Assn., 1897, xxix, 472.
Arneth. München. med. Wchnschr., li, 1993.
Arneth. Die Neutrophilen weissen Blutkörperchen bei Infektionskrankheiten, Jena, 1904.
Löwitt. Zent. f. inner. Med., 1892, 13.
Lepine and Popoff.
Mikulicz. Deutsch. med. Wchnschr., 1904, 1140.
Hahn. Arch. f. Hyg., 1897, 312.
Schauta. Ztschr. f. Gynäk., 1896, No. 17.
Borchardt. Deutsch. med. Wchnschr., 1904, 1806.
Miyake. Mitt. aus d. Grenzgeb. d. Med. u. Chir., 1904, xiii, 719.
Renner. Mitt. aus d. Grenzgeb. d. Med. u. Chir., 1904, xv, 89.

THE LIMITS OF BLEEDING CONSIDERED FROM THE CLINICAL STANDPOINT.[1]

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There has been a tendency of late to overemphasize the importance of blood transfusion methods when in reality there is greater need for a more thorough understanding by the medical profession

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[1] Read before the Semi-annual meeting of the Medico-chirurgical Faculty of Maryland, April 26, 1916.